Journal

Tech Science Press

The Radial Point Interpolation Mixed Collocation (RPIMC) Method For The Solution Of The Reaction-Diffusion Equation In Cardiac Electrophysiology

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Summary

The Radial Point Interpolation Mixed Collocation (RPIMC) method is developed for the solution of the reaction-diffusion equation in cardiac electrophysiology simulations. RPIMC is an efficient and purely meshfree technique which is expected to be a valuable alternative to the Finite Element Method (FEM) for cardiac electrophysiology applications where models with a large number of degrees of freedom and high geometric complexity are commonly employed. We apply the operator splitting technique to decouple the reaction-diffusion equation so that the reaction (cardiac cell dynamics) and diffusion (electrical propagation) terms are solved independently. We evaluate the RPIMC in a simulation of the cardiac action potential (AP) propagation in a two-dimensional human ventricular epicardial square tissue with cell dynamics described by the O´Hara-Rudy model. AP propagation simulated using the RPIMC method is compared against AP propagation simulated with FEM using isoparametric bilinear elements. Comparable results between RPIMC and FEM are obtained for both planar and spiral wave AP propagation, the latter being of interest for investigation of cardiac arrhythmias. The convergence of the RPIMC solution to the FEM solution is evaluated for varying nodal spacing and varying dilatation coefficient during support domain nodes identification.

Keywords: radial point interpolation; mixed collocation; meshfree; cardiac electrophysiology

Introduction

The propagation of the electrical impulse in the human heart is a complex multiscale phenomenon [1] that can be described mathematically by the following reaction-diffusion equation (1a) and boundary condition equation (1b):

$$\partial V/\partial t = -I_{ion}/C + \boldsymbol{\nabla}\cdot(\boldsymbol{D}\boldsymbol{\nabla}V) \quad in\ \Omega, \tag{1a}$$

$$\boldsymbol{n}\cdot(\boldsymbol{D}\boldsymbol{\nabla}V) = 0 \quad on\ \partial\Omega, \tag{1b}$$

where Ω and $\partial\Omega$ are the domain of interest and its boundary, $\boldsymbol{n}$ is the outward unit vector to the boundary, V is the action potential (AP), I_{ion} is the sum of the cardiac cell ionic currents, C is the cell capacitance and $\boldsymbol{D}$ is the diffusion tensor, commonly defined by:

$$\boldsymbol{D} = d_0[(1-\rho)\boldsymbol{f}\otimes\boldsymbol{f} + r\boldsymbol{I}], \tag{2}$$

where d_0 expresses the conductivity coefficient, $\rho \leq 1$ is the transversal to

longitudinal conductivity ratio, $\boldsymbol{f}$ is the fiber direction vector, $\boldsymbol{I}$ is the identity matrix and $\otimes$ denotes the tensor product operation. The diffusion term $\boldsymbol{\nabla} \cdot (\boldsymbol{D}\boldsymbol{\nabla}V)$ describes the propagation of the transmembrane voltage in the tissue, while the reaction term $-I_{ion}/C$ describes the cellular electrical response (action potential, AP). Due to the high complexity of cardiac cell dynamics, realistic AP models are usually defined by a large number of "stiff" ordinary differential equations modeling cardiac ion channel gating and intracellular ionic concentrations [2]. The "stiffness" of the reaction term requires a sufficiently small time integration step to ensure stability and accuracy of the numerical solution of the reaction-diffusion equation (1). To allow for a larger time step without reducing numerical stability and accuracy, the problem can be decoupled by using the operator splitting technique [3] so that the two terms of the reaction-diffusion equation are solved sequentially. A larger time step can then be used for the integration of the diffusion term while the reaction term can be integrated adaptively using a smaller time step. Most state-of-art numerical solvers in cardiac electrophysiology employ the operator splitting approach and use the Finite Element Method (FEM) to derive the numerical solution. However, due to the complexity of the human heart geometry, meshfree methods that alleviate the mesh requirement are of great interest. In this work, we propose the Radial Point Interpolation Mixed Collocation [4] for the simulation of AP propagation in cardiac electrophysiology.

Methodology

The Radial Point Interpolation Mixed Collocation (RPIMC) method is a purely meshfree method based on the Meshless Local Petrov Galerkin (MLPG) method [5, 6], where the Radial Point Interpolation (RPI) is used to construct trial functions and the Dirac delta function is used to construct test functions. Using RPIMC, the weak form of equation (1) is evaluated directly on the discretization nodes of the domain of interest and is given by the following equation (3), while the use of the Dirac delta function to construct test functions reduces the spatial integration of the weak form to nodal summation over the support domain nodes:

$$\sum_{i=1}^{n} \phi^i(\boldsymbol{x_I})\, \partial V^i/\partial t = -I_{ion}(V^I)/C + \sum_{i=1}^{n} \boldsymbol{\nabla} \cdot (\boldsymbol{D}\boldsymbol{\nabla}\phi^i(\boldsymbol{x_I}))V^i, \tag{3}$$

where $\partial V^i/\partial t$ is the time derivative of the action potential at the i^{th} neighbor node, n is the number of nodes in the support domain of the I^{th} discretization node and $\boldsymbol{\phi}^i(\boldsymbol{x_I})$ is the i^{th} component of the RPI basis function given by:

$$\boldsymbol{\phi}^T(\boldsymbol{x_I}) = \{\boldsymbol{r}^T(\boldsymbol{x_I})\ \ \boldsymbol{p}^T(\boldsymbol{x_I})\}\boldsymbol{G}(\boldsymbol{x_I})^{-1}, \tag{4}$$

where $\boldsymbol{r}(\boldsymbol{x_I}) = \left\{r_{I1}^5\ \ r_{I2}^5\ \ \ldots\ \ r_{In}^5\right\}^T$ is the polyharmonic radial basis (RBF) vector proposed in [7], with r_{In} being the radial distance between the n^{th} support domain node $\boldsymbol{x_n}$ and $\boldsymbol{x_I}$ and $\boldsymbol{p}(\boldsymbol{x_I}) = \{1\ \ \boldsymbol{x_I}\}^T$, where $\boldsymbol{x_I} = \{x_I\ \ y_I\}$, denotes the linear polynomial basis. $\boldsymbol{G}(\boldsymbol{x_I})$ is composed by the RBF and polynomial basis moment matrices, $\boldsymbol{R}(\boldsymbol{x_I})$ and $\boldsymbol{P}(\boldsymbol{x_I})$

respectively:

$$\boldsymbol{G}(\boldsymbol{x_I}) = \begin{bmatrix} \boldsymbol{R}(\boldsymbol{x_I}) & \boldsymbol{P}(\boldsymbol{x_I}) \\ \boldsymbol{P}(\boldsymbol{x_I})^T & \boldsymbol{0} \end{bmatrix}. \quad (5)$$

The matrices $\boldsymbol{P}(\boldsymbol{x_I})$ and $\boldsymbol{R}(\boldsymbol{x_I})$ are defined as:

$$\boldsymbol{R}(\boldsymbol{x_I}) = \begin{bmatrix} r_{11}^5 & r_{12}^5 & \dots & r_{1n}^5 \\ & \vdots & & \\ r_{n1}^5 & r_{n2}^5 & \dots & r_{nn}^5 \end{bmatrix} \qquad \boldsymbol{P}(\boldsymbol{x_I}) = \begin{bmatrix} 1 & x_1 & y_1 \\ & \vdots & \\ 1 & x_n & y_n \end{bmatrix} \quad (6)$$

Explicit time integration is performed using the forward Euler method. The operator splitting technique is applied to decouple the solution of equation (3) and, in this way, the solution of equation (3) at a time step k is obtained by:

a. Solving $\partial V_I^{k\prime}/\partial t = -I_{ion}(V_I^{k-1})/C$, and then
b. Solving $\sum_{i=1}^{n} \phi^i(\boldsymbol{x_I})\, \partial V_i^k/\partial t = \sum_{i=1}^{n} \nabla \cdot (D \nabla \phi^i(\boldsymbol{x_I})) V_i^{k\prime}$.

In this study, we consider electrical propagation in a two-dimensional human ventricular epicardial tissue. The O'Hara Rudy model [2] is used to describe cell dynamics in step *a.* of the decoupled RPIMC solution.

Numerical examples

In the first example, we consider a 5 cm x 5 cm human ventricular epicardial tissue. The cardiac fibers direction is considered perpendicular to the X-axis ($\boldsymbol{f} = [1 \;\; 0]^T$). We use a conductivity coefficient $d_0 = 0.0013\ mS/cm$ and transversal to longitudinal conductivity ratio $\rho = 1/4$. Periodic stimuli with period $t_T = 1\ s$, duration $t_d = 2\ ms$ and amplitude (A) of twice diastolic threshold are applied on the left side of the tissue ($x = 0\ cm$). The AP propagation is simulated for time $t_s = 3\ s$. We validate the solution of the RPIMC method by comparing it with a FEM solution using bilinear isoparametric elements. We consider regular nodal discretizations and quadrilateral meshes with nodal spacing $h = \{0.2, 0.1, 0.05, 0.025\}\ cm$. The support domain size $s_d = \alpha\, h$, with $\alpha = 2.8$, is used for the support domain construction in RPIMC. A comparison of the generated APs by RPIMC and FEM in the time interval $t = [0\ 3]\ s$ for all the tested nodal discretizations is given in Figure 1. To further evaluate the simulated APs we measure the AP duration (APD) for 90%, 50% and 20% repolarization. The APD_{90} metric denotes the duration between the time corresponding to the maximum derivative of transmembrane voltage and the time to complete 90% repolarization. The APD_{50} and APD_{20} metrics are defined similarly for 50% and 20% repolarization. The highest value of the percentage difference between the RPIMC APD compared to the FEM APD is found to be 0.45%, 2.25%, and 2.27% for APD_{90}, APD_{50}, APD_{20} and nodal spacing $h = 0.2\ cm$. The percentage error is reduced monotonically when diminishing the nodal spacing and is equal to zero for nodal spacing $h = 0.025\ cm$. We investigate the effect of the dilatation coefficient α by computing the Normalized Root Mean Square (NRMS) error between the RPIMC and FEM solutions at $t = 2.2\ s$ for a nodal discretization with $h = 0.04\ cm$ and varying dilatation coefficient $\alpha = \{1.2, 1.6, 2.0, 2.4, 2.8\}$.

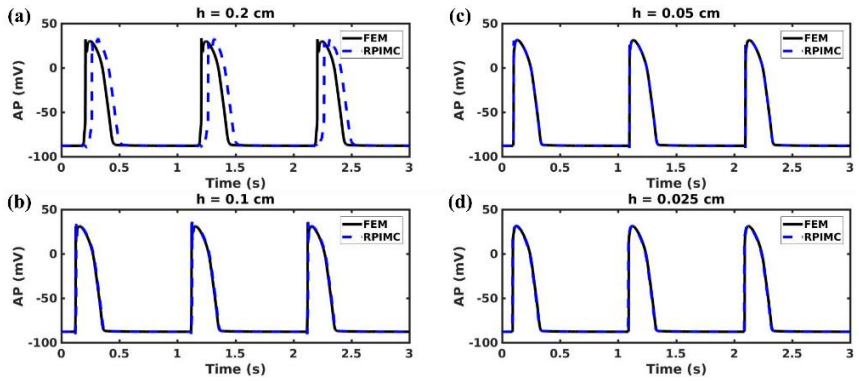

Figure 1. Comparison of simulated APs in the time interval $\boldsymbol{t} = [\mathbf{0}\ \mathbf{3}]\ \boldsymbol{s}$ for nodal spacing (a) $\boldsymbol{h} = \mathbf{0.2}\ \boldsymbol{cm}$, (b) $\boldsymbol{h} = \mathbf{0.1}\ \boldsymbol{cm}$, (c) $\boldsymbol{h} = \mathbf{0.05}\ \boldsymbol{cm}$, (d) $\boldsymbol{h} = \mathbf{0.025}\ \boldsymbol{cm}$.

The NRMS error is computed using the formula:

$$NRMS = \frac{\left(\sum_{x_j \in \Omega}\left(V^{RPIMC}(\boldsymbol{x_j}) - V^{FEM}(\boldsymbol{x_j})\right)^2\right)^{1/2}}{max\left|V^{FEM}(\boldsymbol{x_j})\right| - min\left|V^{FEM}(\boldsymbol{x_j})\right|}, \tag{7}$$

where $\boldsymbol{x_j}$ is the j^{th} node in the discretization of the domain Ω, $V^{RPIMC}(\boldsymbol{x_j})$ is the RPIMC solution at $\boldsymbol{x_j}$, and $V^{FEM}(\boldsymbol{x_j})$ is the FEM solution at $\boldsymbol{x_i}$. The NRMS error convergence plot with respect to α is given in Figure 2.

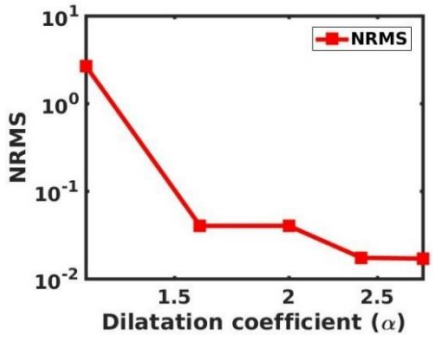

Figure 2. Normalized Root Mean Square (NRMS) error convergence for varying dilatation coefficient $\boldsymbol{a} = \{\mathbf{1.2}\ \mathbf{1.6}\ \mathbf{2.0}\ \mathbf{2.4}\ \mathbf{2.8}\}$ and nodal spacing $\boldsymbol{h} = \mathbf{0.04}\ \boldsymbol{cm}$

In the next example, an S1-S2 cross stimulation protocol [8] is simulated to investigate the ability of RPIMC to generate and maintain spiral wave dynamics, of high interest for investigation of cardiac arrhythmias. The same tissue geometry and parameter values as in the previous example are used, being nodal spacing $h = 0.025\ cm$. An initial stimulus (S1) is applied at the left edge of the tissue ($x = 0\ cm$) at time $t = 50\ ms$. A second stimulus (S2) is applied at a square region located at the left bottom corner of the tissue with a width of $1.25\ cm$ and height of $2.50\ cm$ at time $t = 290\ ms$. If spiral waves generated due to the interaction of the S2 wave front with the S1 wave tail are such that at least 2 spirals are generated until time $t_s = 1\ s$, the spiral wave is considered to be sustained. Results obtained using RPIMC and FEM at different time intervals are plotted in

Figure 3. Sustained spiral waves of high similarity are generated both for RPIMC and FEM. The degradation of the similarity between RPIMC and FEM spiral waves with time may be associated with the slightly slower conduction velocity of the AP in the FEM simulation as compared to RPIMC simulation.

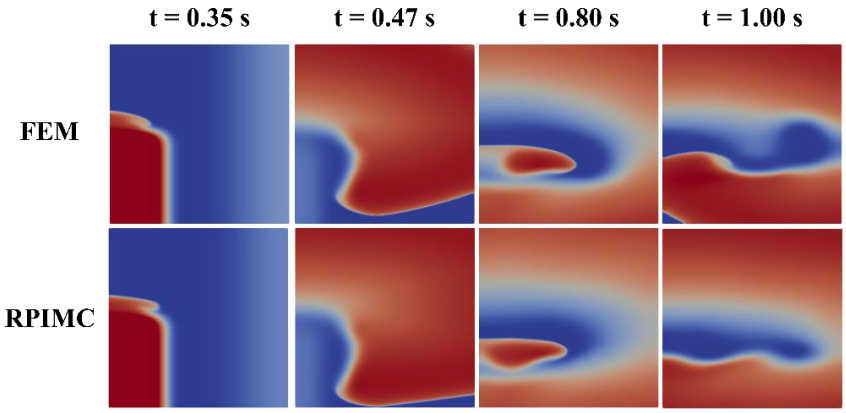

Figure 3. Spiral wave propagation at different instants in the time interval $\boldsymbol{t} = [\mathbf{0}\ \mathbf{1}]\ \boldsymbol{s}$ for the S1-S2 cross stimulation protocol.

References

1. Pueyo, E., Corrias, A., Virág, L., Jost, N., Szél, T., Varró, A., Szentandrássy, N., Nánási, P.P., Burrage, K. and Rodríguez, B. (2011). A multiscale investigation of repolarization variability and its role in cardiac arrhythmogenesis. *Biophysical journal*, *101*(12), 2892-2902.
2. O'Hara, T., Virág, L., Varró, A. and Rudy, Y. (2011). Simulation of the undiseased human cardiac ventricular action potential: model formulation and experimental validation. *PLoS computational biology*, *7*(5), 1002061.
3. Qu, Z. and Garfinkel, A. (1999). An advanced algorithm for solving partial differential equation in cardiac conduction. *IEEE Transactions on Biomedical Engineering*, *46*(9), 1166-1168.
4. Mountris, K.A. and Pueyo, E. (2020). The Radial Point Interpolation Mixed Collocation (RPIMC) Method for the Solution of Transient Diffusion Problems. *arXiv preprint arXiv: 2001.01027*.
5. Atluri, S.N. and Zhu, T. (1998). A new meshless local Petrov-Galerkin (MLPG) approach in computational mechanics. *Computational mechanics*, *22*(2), 117-127.
6. Zhang, T., He, Y., Dong, L., Li, S., Alotaibi, A. and Atluri, S.N. (2014). Meshless local petrov-galerkin mixed collocation method for solving cauchy inverse problems of steady-state heat transfer. *CMES: Computer Modeling in Engineering & Sciences*, *97*(6), 509-553.
7. Liu, G.R. and Gu, Y.T. (2005). *An introduction to meshfree methods and their programming*. Springer Science & Business Media.
8. Gomez, J.F., Cardona, K., Martinez, L., Saiz, J. and Trenor, B. (2014). Electrophysiological and structural remodeling in heart failure modulate arrhythmogenesis. 2D simulation study. *PloS one*, *9*(7), 103273

Acknowledgements

This work was supported by the European Research Council under the grant agreement ERC-2014-StG 638284, by MINECO (Spain) through project DPI2016-75458-R and by European Social Fund (EU) and Aragón Government through BSICoS group (T3917R) and project LMP124-18. Computations were performed by the ICTS NANBIOSIS (HPC Unit at University of Zaragoza)